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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/940,544	09/30/1997	MICHEL SADELAIN	MSK.P-035-US	5042

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EXAMINER
HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
1642	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/940,544	SADELAIN ET AL.	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *8-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6 and 7* is/are rejected.

7)☒ Claim(s) *3-5* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 8-20 are withdrawn from consideration.

Claims 1-7 are under examination.

2. The text of those sections of title 35, USC Code not included on the Office Action can be found in a prior Office Action.

3. The following Office Action contains some NEW GROUNDS of rejections.

Rejection Withdrawn

4. The rejection of claims 1-7 under 35 U.S.C. 103(a) as being unpatentable over Cheung et al et al (WO 97/34634, published 9/25/97, Information Disclosure Statement filed 6/3/98), and further in view of Alvarez-Villina et al (Eur. J. Immunol. (1996) 26:2304-209, Information Disclosure Statement filed 6/3/98) and Sambrook et al (Molecular Cloning A Laboratory Manual, Cold Spring Harbor Laboratory, 1989) is withdrawn in view of the declaration signed by all inventors as paper #26 and 22 ½ .

5. The rejection of claims 1-3 under 35 U.S.C. 103(a) as being unpatentable over Cheung et al and further in view of Alvarez-Vallina et al is withdrawn in view of the declaration signed by all inventors as paper #26 and 22 ½.

6. The rejection of claims 1-2 under 35 U.S.C. 102(a) as being anticipated by Alvarez-Vallina et al (Eur. J. Immunol. (10/1996) 26, pp 2304-2309, Information Disclosure Statement, filed 6/3/98) is withdrawn in view of the declaration signed by all inventors as paper #26 and 22 ½.

7. The rejection of claims 1-7 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 2 of copending Application No. 09/142974 in view of Alvarez-Vallina et al and Sambrook et al was withdrawn in the previous Office Action.

8. The rejection of claims 1-3 under 35 U.S.C. 103(a) as being unpatentable over Eshhar et al (WO 93/19163, published 9/30/93) and further in view of Fouser et al (WO 92/18629) is withdrawn in view of arguments.

9. The rejection of claims 1-7 under 35 U.S.C. 103(a) as being unpatentable over Eshhar et al (WO 93/19163, published 9/30/93) and further in view of Fouser et al (WO 92/18629, published 10/29/92) and Sambrook et al (Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, 1989) is withdrawn in view of arguments.

10. The rejection of claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts (U.S. Patent 5,686,281, filed 5/1995, IDS #24) as applied to claims 1-2 above, and further in view of Fouser et al (WO 92/18629, published 10/92) and Sambrook et al (Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, 1989) is withdrawn in view of arguments.

Response to Arguments

11. The rejection of claims 1-2 under 35 U.S.C. 102(b) as being anticipated by Eshhar et al (WO 93/19163, published 9/30/93) is maintained.

The response filed 4/15/03 has been carefully considured but is deemed not to be persuasive. The response states that the reference is not enabled and does not place it in position of a person of ordinary skill in the field and that the examiner has not offered any reason why CD16 and CD28 would be similar (see page 2-4 of response). In response to these arguments, Eshhar clearly teaches fusion proteins with an antibody and CD28 (see page 7-8). The claims are directed to polynucleotides and it was routine in the art at the time the invention was made to produce polynucleotides of fusion protein and as evidenced from Eshhar a ScFv-CD16 polynucleotide was made. In addition, Eshhar et al teach fusion proteins of SCFv-CD16 that are functional and it was routine in the art at the time of the claimed invention to produce fusion proteins and as taught by Eshhar the ScFv-CD16 was functional.

12. The rejection of claims 1-2 under 35 U.S.C. 102(e) as being anticipated by Roberts (U.S. Patent 5,686,281, filed 5/1995, IDS #24) is maintained.

The response filed 4/15/03 has been carefully considured but is deemed not to be persuasive. The response argues that the patent provides no examples or how to make the fusion proteins. In response to these arguments, the claims require a polynucleotide and it was routine in the art at the time the invention was made to produce polynucleotides of fusion protein.

The following is some NEW GROUNDS of rejections

Claim Rejections - 35 USC § 103

13. Claims 1-2, 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Eshhar et al (WO 93/19163, published 9/30/93) as applied to claims 1-2 above and further in view Sambrook et al (Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, 1989).

The claims are drawn to a recombinant polynucleotide encoding a fusion protein comprising the variable region of the light chain linked to the variable region of the heavy chain of a single chain antibody, signal domain of human CD28 receptor and a human transmembrane domain, further comprising a suicide gene encoding thymidine kinase.

Eshhar et al teach polynucleotides encoding CD28 fusions with a single chain antibody. Eshhar et al does not teach a polynucleotide further comprising a gene encoding thymidine kinase. This deficiency is made up for in the teachings of Sambrook et al.

Sambrook et al teach the thymidine kinase gene, which is expressed in most mammalian cells (Page 16.9). Sambrook et al also teach a plasmid, pTK2, which carries a fragment of the herpes simplex virus (HSV) encoding thymidine kinase (tk) (see page 16.11, Figure 16.1A).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to produce a polynucleotide encoding a fusion

protein comprising a single chain antibody and a signaling domain of human CD28 and human CD28 transmembrane domain and a gene coding for thymidine kinase.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to produce a polynucleotide encoding a fusion protein comprising a single chain antibody and a signaling domain of human CD28 and human CD28 transmembrane domain and a gene coding for thymidine kinase because Sambrook et al teach a medium containing hypoxanthine, aminopterin, and thymidine (HAT medium) "in which only cells expressing the tk gene will grow. Thus, by using the appropriate medium it is therefore possible to select for cells expressing the tk gene". Thus, it would have been obvious to combine the teaching of Eshhar et al for producing a polynucleotide encoding for a fusion protein of a single chain antibody and the signaling and transmembrane domains of CD28 and further combine this polynucleotide with a polynucleotide encoding the thymidine kinase protein of Sambrook et al for selection of cells expressing the polypeptide.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art a the time the invention was made, as evidenced by the references.

14. Claims 1-2, 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts (U.S. Patent 5,686,281, filed 5/1995, IDS #24) as applied to claims 1-2 above and further in view Sambrook et al (Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory, 1989).

The claims have been described supra.

Roberts teach polynucleotides that encode human CD28 cytoplasmic and transmembrane domains fused to a single-chain antibody (see column 6, lines 55-67). Roberts does not teach a polynucleotide further comprising a gene encoding thymidine kinase. This deficiency is made up for in the teachings of Sambrook et al.

Sambrook et al has been described supra.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to produce a polynucleotide encoding a fusion protein comprising a single chain antibody and a signaling domain of human CD28 and human CD28 transmembrane domain and a gene coding for thymidine kinase.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to produce a polynucleotide encoding a fusion protein comprising a single chain antibody and a signaling domain of human CD28 and human CD28 transmembrane domain and a gene coding for thymidine kinase because Sambrook et al teach a medium containing hypoxanthine, aminopterin, and thymidine (HAT medium) "in which only cells expressing the tk gene will grow. Thus, by using the appropriate medium it is therefore possible to select for cells expressing the tk gene". Thus, it would have been obvious to combine the teaching of Roberts et al for producing a polynucleotide encoding for a fusion protein of a single chain antibody and the signaling and transmembrane domains of CD28 and further combine this polynucleotide with a polynucleotide encoding the thymidine kinase protein of Sambrook et al for selection of cells expressing the polypeptide.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art a the time the invention was made, as evidenced by the references.

Conclusions

15. No Claims are allowed. Claims 3-5 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

17. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the

Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

Respectfully,

Larry R. Helms Ph.D.

703-306-5879